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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/939,230	08/24/2001	Alan David Wickenden	018512-006610US	5203

20350 7590 09/21/2009

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EXAMINER	
ROYDS, LESLIE A	

ART UNIT	PAPER NUMBER
1614	

MAIL DATE	DELIVERY MODE
09/21/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/939,230	WICKENDEN ET AL.	
	Examiner	Art Unit	
	LESLIE A. ROYDS	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 July 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *45-57,60-62,65-69 and 83* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *45-57,61,66,68 and 69* is/are rejected.

7)☒ Claim(s) *60,62,65-69 and 83* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *23 July 2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 45-57, 60-62, 65-69 and 83 are presented for examination.

A request for continued examination under 37 C.F.R. 1.114, including the fee set forth in 37 C.F.R. 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 C.F.R. 1.114, and the fee set forth in 37 C.F.R. 1.17(e) has been timely paid, the finality of the previous Office Action has been withdrawn pursuant to 37 C.F.R. 1.114. Applicant's payment and submission filed July 10, 2009 has been received and entered into the present application. Accordingly, prosecution has been reopened.

Applicant's Information Disclosure Statement (IDS) filed July 23, 2009 has been received and entered into the present application. As reflected the attached, completed copy of form PTO/SB/08A&B (one page total), the Examiner has considered the cited references.

Claims 45-57, 60-62, 65-69 and 83 remain pending and under examination.

Applicant's arguments, filed July 10, 2009, have been fully considered. Rejections not reiterated from previous Office Actions are hereby withdrawn. The following rejections and objections are either reiterated or newly applied. They constitute the complete set of rejections and objections presently being applied to the instant application.

Objection to the Claims (New Grounds of Objection)

Claims 66 and 68-69 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Specifically, each of claims 66 and 68-69 define a compound of the formula instantly claimed wherein Ar^2 is a substituted pyridyl moiety. However, instant claim 65 (from which each of claims 66 and 68-69 ultimately depends) specifies that the Ar^2 is an *un*substituted pyridyl moiety. As a result, the subject matter of instant claims 66 and 68-69 fails to further limit the subject matter of parent claim 65. Applicant is required to cancel the claim(s), or

amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claims 60, 62, 65, 67 and 83 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim Rejections - 35 USC § 112, Second Paragraph (New Grounds of Rejection)

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 66 and 68-69 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Present claim 65 is directed to the method of claim 62, wherein Ar^2 is unsubstituted pyridyl. Present claim 66 is directed to the method of claim 65, wherein Ar^2 is selected from the group consisting of 6-methyl-3-pyridyl and 2-chloro-5-pyridyl (i.e., substituted pyridyl).

In particular, it is unclear how instant claims 66 and 68-69 are intended to further limit the subject matter of parent claim 65, since instant claim 65 specifies that the pyridyl group is unsubstituted and instant claim 66 specifies particular types of substituted pyridyl groups as options for Ar^2. In other words, the recitation of substituted pyridyl groups in instant claim 65 clearly contradicts the subject matter of instant claim 62, which specifies that the pyridyl group is unsubstituted. In addition, the compounds circumscribed by instant claims 68-69 are also directed to compounds wherein Ar^2 is substituted pyridyl. For this reason, Applicant has failed to clearly, precisely or deliberately set forth the metes and bounds of the subject matter for which he is presently seeking protection. Clarification is required.

For these reasons, the claims fail to meet the tenor and express requirements of 35 U.S.C. 112, second paragraph, and are, thus, properly rejected.

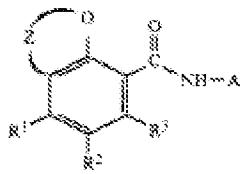
Claim Rejections - 35 USC § 103 (New Grounds of Rejection)

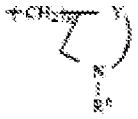
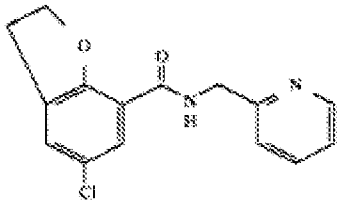
The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 45-57 and 61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Imondi (U.S. Patent No. 5,114,947; 1992) in view of Sudilovsky et al. (U.S. Patent No. 4,931,430; 1990).

Imondi teaches benzofuran-7-carboxamide compounds effective for alleviating anxiety via a strong anxiolytic activity (col.1, l.1-10) of the formula  (col.2, l.20-30), wherein Z represents the carbon and hydrogen atoms necessary to complete a substituted or unsubstituted, saturated or unsaturated, 5- to 7-membered ring (col.2, l.32-34); R^1, R^2 and R^3 may be the same or different and

represent, *inter alia*, hydrogen, lower alkyl, lower alkoxy, halogen or nitro (col.2, l.34-38); and further wherein A is selected from, *inter alia*,  or  (col.2, l.51-68), wherein n is 0 or an integer from 1-3 (col.3, l.36-37); W represents either a single bond or the carbon and hydrogen atoms necessary to complete a 3- to 8-membered saturated or an unsaturated ring and Y represents a single bond or the carbon and hydrogen atoms necessary to complete a 4- to 8-membered saturated or unsaturated ring (col.3, l.23-28); and R6 is, *inter alia*, hydrogen (col.3, l.28). Imnodi further discloses representative compounds according to the invention, including, *inter alia*, the compound identified as (63), which has the structure  (which corresponds to Applicant's instantly claimed compounds wherein X is oxygen, Ar^1 is a benzofuranyl substituted with halogen and Ar^2 is unsubstituted pyridyl; see Imondi, col.14). Imondi teaches a method for treating anxiety comprising administering to a patient in need of such treatment an anxiolytically effective amount of a compound of the type disclosed (col.2, l.17-20), wherein the composition may be administered orally or parentally (including intravenous administration as disclosed at col.25, l.29-33) and may be formulated in combination with diluents, carriers or adjuvants known in the art (col.24, l.43-48). Imondi further teaches that the disclosed compounds are generally effective in amounts of from about 0.001 mg to about 60 mg per patient per day, but indicates that the dosage should be limited to the smallest effective amount in elderly and debilitated patients (i.e., understood to be a "human" as required by Applicant's instant claim 48; col.26, l.50-54).

Note that the teaching of the disclosed compounds in amounts of from about 0.001 mg to about 60 mg per patient per day meets Applicant's instantly claimed dosage amounts of instant claim 54 (i.e.,

0.1 mg/kg-200 mg/kg as recited in instant claim 54) because, for a human being of an average weight of 70 kg, the instantly claimed dosage amounts would range from 7 mg-14000 mg as in instant claim 54, which clearly falls within the range disclosed by Imondi, absent factual evidence to the contrary.

Though it is recognized that the representative compound (63) as disclosed by Imondi differs from Applicant's instant claims in that is contains a $-CH_2-$ group between the -NH group and the pyridyl group, it is noted that Imondi explicitly teaches that the groups identified as options for "A" may be directly bonded to the –NH group without an alkylene linker as evidenced by the fact that Imondi discloses that n may be 0 or an integer from 1-3 (i.e., if n is 0, then no alkylene linker is present and the "A" group is directly attached to -NH). Thus, though this feature of an absent alkylene linker is not specifically exemplified in this representative compound of the reference, it would have been apparent to one of ordinary skill in the art that Imondi defined n as a list of alternative options, i.e., 0, 1, 2 or 3. This clear disclosure of each option for n alternatively is an explicit teaching that n may be varied with the disclosed parameters and still circumscribe a compound according to the invention. Thus, the motivation to vary n (in this case, to elect n=0 such that the alkylene linker is absent as required by the instant claims) such as, e.g., to arrive at the instantly claimed compound, is clearly derived from the disclosure of n as a list of alternative options, each of which may be individually selected and each of which is disclosed as equally operative to form a compound with strong anxiolytic activity, absent factual evidence to the contrary.

Furthermore, though Imondi fails to teach that the disclosed compound(s) function to increase ion flow through KCNQ potassium channels in a cell (claim 45), such as where the KCNQ channel is either heteromeric or homomeric (claims 49-50) and/or that the channel is heteromeric and contains a KCNQ2 and/or KCNQ3 polypeptide subunit (claims 51-53), such properties would have been reasonably expected to be present in the compound(s) disclosed by Imondi because Imondi teaches compound(s) that appear to be *prima facie* identical to those instantly claimed for the same therapeutic purpose to that instantly

claimed (i.e., for the treatment of anxiety in a subject in need thereof) and, thus, must also reasonably possess these same newly cited properties regarding increasing ion flow through KCNQ potassium channels as alleged by Applicant, absent factual evidence to the contrary. Applicant is reminded that a chemical composition and its properties are inseparable such that products of identical chemical composition, particularly when used in the same manner (i.e., administration of the same compound to the same host for the same therapeutic purpose) cannot have mutually exclusive properties. Please see MPEP §2112.

In re Best (195 USPQ 430) and *In re Fitzgerald* (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter, which there is reason to believe includes functions and/or properties that are newly cited, or is identical to a product instantly claimed. In such a situation the burden is shifted to the Applicants to "prove that subject matter to be shown in the prior art does not possess the characteristic relied on" (205 USPQ 594, second column, first full paragraph). There is no requirement that a person of ordinary skill in the art would have recognized the newly cited function and/or property at the time of invention, so long as the function and/or property can be demonstrated to be reasonably expected to be present. *Schering Corp. v. Geneva Pharm. Inc.*, 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003); see also *Toro Co. v. Deere & Co.*, 355 F.3d 1313, 1320, 69 USPQ2d 1584, 1590 (Fed. Cir. 2004) ("[T]he fact that a characteristic is a necessary feature or result of a prior-art embodiment (that is itself sufficiently described and enabled) is enough for inherent anticipation, even if that fact was unknown at the time of the prior invention"). See MPEP §2112.

Imondi fails to specifically teach the treatment of anxiety caused by panic disorder, generalized anxiety disorder, or stress disorder (claim 46), such as acute stress disorder or post-traumatic stress disorder (claim 47), or the specifically claimed dosage amount of 10-100 mg/kg (claim 55).

Sudilovsky et al. teaches disorders associated with anxiety effectively treated using an anti-anxiety therapy (col.1, l.43-48), including chronic and acute anxiety disorders, post-traumatic stress disorder, and generalized anxiety disorder (col.1, l.49-57).

In view of such teachings, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to employ the anti-anxiety compounds of Imondi for the treatment of other disorders characterized by anxiety, including chronic and acute anxiety disorder, generalized anxiety disorder and/or post-traumatic stress disorder, as evidenced by Sudilovsky et al., for the treatment of the anxiety associated with such disorders. Such compounds would have been reasonably expected to exert the same or substantially equivalent efficacy in the treatment of these anxiety disorders in a patient in need of such treatment because: (1) the compounds of Imondi were known to have efficacy in treating patients that suffer from anxiety *per se* (i.e., anxiety of any etiology) and (2) Sudilovsky et al. teaches various disorders associated with anxious manifestations (e.g., chronic and acute anxiety disorders, post-traumatic stress disorder, and generalized anxiety disorder). In other words, Imondi provides the clear teaching that the instantly claimed compound(s) is, in fact, effective for treating all anxiety patients, i.e., 100% of patients with anxiety, without exclusion, and, accordingly, the suggestion of Imondi to use the disclosed compounds and formulations thereof for treating any anxiety patient is a clear suggestion to use it in any subpopulation of patients suffering from anxiety disorders, such as those patients suffering from chronic and acute anxiety disorders, post-traumatic stress disorder, and generalized anxiety disorder, with the reasonable expectation of the same (or at least substantially equivalent) level of efficacy in treating such patients with chronic and acute anxiety disorders, post-traumatic stress disorder, and/or generalized anxiety disorder as would be expected in the treatment of anxiety patients *per se* because of the therapeutic anti-anxiety effects of the compounds of Imondi.

Regarding the instantly claimed dosage range of 10-100 mg/kg (claim 55), Imondi expressly teaches that, "As used herein, the term "anxiolytically effective amount" refers to the concentration of the

active drug substance in a pharmaceutically acceptable as well as biologically acceptable pharmaceutical dosage form effective to reduce or alleviate anxiety in a patient suffering from such condition. Such amount will vary from patient to patient depending on such factors as body weight, age, overall general health as well as a consideration of any other medications being administered to the patient at the same time." See Imondi, col.25, l.39-49.

It is obvious from the above teachings that Imondi expressly contemplates variation in the dosage amounts of the disclosed compounds and specifically acknowledges that such a matter was well within the skill of the artisan at the time of the invention and would not have required undue experimentation or have been outside the realm of knowledge generally available to the skilled artisan. Factors that would have been taken into consideration when making such a determination would have included, but not have been limited to, the age, weight, sex, diet and medical condition of the patient, severity of the disease, route of administration, pharmacological considerations, e.g., activity, efficacy, pharmacokinetics and toxicology profiles of the particular compound employed, whether a drug delivery system is utilized and whether the compound is administered as part of a drug combination. Thus, the dosage regimen that would have actually been employed would have been expected to vary widely and, in the absence of evidence to the contrary, would not have been inconsistent with that which is presently claimed.

In addition, the concentration of the active ingredient is a result-effective variable, i.e., a variable that achieves a recognized result and, therefore, the determination of the optimum or workable dosage range would have been well within the practice of routine experimentation by the skilled artisan, absent factual evidence to the contrary, and, further, absent any evidence demonstrating a patentable difference between the compositions used and the criticality of the amount(s).

Conclusion

Rejection of claims 45-57, 61, 66 and 68-69 is proper.

Claims 60, 62, 65, 67 and 83 are objected to for depending from a rejected base claim.

No claims of the present application are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leslie A. Royds whose telephone number is (571)-272-6096. The examiner can normally be reached on Monday-Friday (9:00 AM-5:30 PM).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571)-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leslie A. Royds/
Patent Examiner, Art Unit 1614

September 15, 2009

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614